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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,868	08/11/2006	Roghieh Saffie	2491-66	4844

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EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,868	SAFFIE ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 2, 4 - 9, 13, 14, 18, 20, 21* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4 - 9, 13, 14, 18, 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed March 12, 2009, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1, 2, 4 - 6 and 13 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16 and 19 – 21 of copending Application No. 10/468742. This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 15, 2008 and those set forth.

Applicant's request that this provisional rejection be held abeyance until an indication of allowable subject matter is made.

Therefore, the rejection is maintained for the reasons of record previously set forth.

Claim Objections

3. Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Amended claim 1 requires a silicon carrier material. Claim 2 fails to further limit claim 1 as the germanium material recited in the Markush group of claim 2 does not contain silicon and therefore is not a porous silicon carrier material.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 2, 4, 6, 8, 9, 13, 14, 18 and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Canham et al. (WO 02/067998) in view of Nsereko et al. (Biomaterials 2002). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 15, 2008 and those set below.

Applicant traverses this rejection on the grounds that Nsereko does not provide the missing motivation to arrive at the present invention of injection directly into the tumor and using paclitaxel as the cytotoxic agent. Nsereko is concerned with an entirely different carrier material and the average skilled reader would not consider the teachings of Nsereko et al. relevant to products using a silicon delivery vehicle. Even if such a person did look to Nsereko, they would have no reason to predict the advantage provided by this formulation that allows for the site-specific administration of cytotoxic drugs at dosage levels in excess of the LD_{50} of the free drug without significant mortality. The advantages of the porous silicon carrier recited in Canham do not

suggest this advantage of allowing such a high drug dose. The Examiner's arguments regarding no evidence that the dosages being delivered from the microparticles of Canham has no basis other than hindsight based on the knowledge of the present invention.

These arguments are not found persuasive. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Canham et al. discloses internal therapeutic particles that can contain cytotoxic drugs based on silicon material. The carrier allows for site-specific release of the cytotoxic drug (p 4, ln 28 – 31). Nsereko et al. also discloses localized delivery of paclitaxel using a different material (chitin) as the carrier material, and specifically discusses the disadvantages of the delivery of the cytotoxic agents through the vasculature system (p 2723, col 1, ¶ 1). The particles of Canham et al. are administered to the hepatic artery so delivery of the particles is still limited by the vasculature of the tumor, a deficiency explicitly discussed by Nsereko et al. that can be remedied by direct injection into the tumor. Thus, despite the differences in materials used, both Canham et al. and Nsereko et al. deal with the treatment of cancer by administration of

microparticles which can degrade over time that contain a cytotoxic drug and thus one of ordinary skill in the art would combine the teachings of these two references as they address the same problem using similar drug delivery strategies. The chitin microparticles of Nsereko et al. and the silicon microparticles of Canham et al. can thus be viewed as functionally equivalent in that they are degradable microparticles capable of carrying and delivering cytotoxic agents to a particular location.

One of ordinary skill would know that higher concentrations of cytotoxic agents would kill more cancer cells, but if such doses where administered systemically, those higher concentrations would also kill more non-cancerous skills and be accompanied by increased side effects. By localizing the dosage form, a much higher dosage of active ingredient can be administered with fewer side effects than seen with systemic administration (p 2723, col 2, ¶ 1 of Nsereko et al.) and paclitaxel is a prime candidate for localized delivery (p 2723, col 2, ¶ 2). Thus, a dose higher than the LD_{50} of the free drug can be administered locally to kill more cancer cells without the potentially lethal side effects associated with a systemic administration of the same drug dose.

8. Claims 1, 2, 4 – 6, 8, 9, 13, 14, 18 and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Canham et al. and Nsereko et al. further in view of Canham et al. (US 6,322,895). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 15, 2008 and those set forth below.

Applicant traverses this rejection on the basis that at best this combination of references leads to average skilled person to consider using mesoporous silicon as a

porous carrier material and there still would be no motivation to consider direct intratumor administration and no expectation that the delivery of dosages which are significantly greater than the LD_{50} could be achieved.

These arguments are not persuasive. As discussed in greater detail above, Nsereko et al. does provide motivation for direct intratumor administration method and delivery of dosages greater than the LD_{50} value. Canham '895 indicates that mesoporous silicon can used as resorbable porous material which can be used for drug delivery, and is thus functionally equivalent to the silicon materials discussed in Canham '998.

9. Claims 1, 2, 4, 6 – 9, 13, 14, 18 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canham et al. (WO 02/067998) in view of Straub et al. (US 6,610,317). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 15, 2008.

Applicant traverses this rejection on the grounds that although Straub describes paclitaxel in porous matrix form, the matrix comprises hydrophilic excipients and a wetting agent and there is no disclosure of a porous silicon carrier. The average skilled man looking to provide an alternative formulation and method to Canham '998 would not look to Straub for guidance.

These arguments are not persuasive. Canham '998 discloses the use of a porous matrix material for the site-specific delivery of cytotoxic agents. Straub et al. discloses the use of a porous matrix material for the site-specific delivery of the

cytotoxic agent. Thus, one of ordinary skill in the art, in reading Straub, would realize that paclitaxel is a cytotoxic drug that can be loaded onto/into a porous matrix material and used in a method of treating cancer. While the porous material utilized by the two references are different, the general principle of drug delivery, the class of drugs being used and the method in the which the drug delivery particles are used is the same between the two references and thus one of ordinary skill in the art would be motivated to prepare porous silicon particles loaded with paclitaxel and use them to treat cancer.

10. Claims 1, 2, 4 – 9, 13, 14, 18 and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Canham et al. and Straub et al. further in view of Canham et al. (US 6,322,895). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 15, 2008 and those set forth below.

Applicant traverses this rejection on the grounds that Canham '895 does not provide the missing motivation.

This argument is not persuasive. As discussed, motivation to combine Canham '998 and Straub so Canham '895 does need to provide that motivation. Therefore this rejection is maintained for the reasons of record previously set forth.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW